Micro Platform for Controlled Cardiac Myocyte Differentiation

Grant Award Details

Micro Platform for Controlled Cardiac Myocyte Differentiation

Grant Type: SEED Grant

Grant Number: RS1-00239-B

Investigator:

Name:	Michelle Khine
Institution:	University of California, Irvine
Type:	PI

Disease Focus: Heart Disease

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $156,426

Status: Closed

Progress Reports

Reporting Period: Year 2

View Report

Reporting Period: Year 2 NCE

View Report

Grant Application Details

Application Title: Micro Platform for Controlled Cardiac Myocyte Differentiation

Public Abstract:

Congestive heart failure, the inability of the heart to continue to pump effectively due to damage of its muscle cells, affects approximately 4.8 million Americans and is a leading cause of mortality. Causes of the irreversible damage to the cardiomyocytes that results in congestive heart failure include hypertension, heart attacks, and coronary disease. Because the cadiomyocytes in the adult heart tissue are terminally differentiated and thus cannot regenerate themselves, once they are damaged, they are irreversibly damaged. As a consequence, despite the advances in medical devices and pharmaceuticals, still more than 50% of congestive heart failure patients die within 5 years of initial diagnosis.

The goal therefore must be to restore the heart cells' functions. This is possible by transplanting fetal and neonatal cardiomyocytes which can then integrate into the host tissue. This approach has demonstrated success in improving heart function. However, the limited availability of fetal donors has prevented its adoption as a viable therapeutic approach.

Embryonic stem cells can overcome this challenge as they proliferate continuously in vitro and can be furthermore stimulated to differentiate. Embryoid bodies are three-dimensional clusters of heterogenous stem cells, some of which contain cardiac myocytes, which demonstrate characteristic spontaneous contractions. Controlled and efficient differentiation of the stem cells into cardiomyocytes and an effective way to characterize/verify these cells is critical. Ensuring a pure population of cardiac myocytes is essential because otherwise there is a high-likelihood of tumor formation when transplanted. Previous studies have shown that a low percentage of all embryoid bodies spontaneously form cardiomyocytes.

Our goal is to therefore develop a self-contained system to grow and controllably differentiate the human embryonic stem cells into cardiomyocytes in high-yields. Few studies have characterized the types of cardiac myocytes in the differentiating human EBs. Our strategy is to use electrical and chemical cues to induce the high-yield differentiation of stem cells into cardiomyocytes and to monitor this process over time both electrically and optically.

Statement of Benefit to California:

Improvements in differentiating stem cells into homogenous populations of specific cell types are much needed for transplantation therapy in general—and for congestive heart failure patients in particular. The benefits associated with the development of this micro platform have even broader reaching implications beyond biomedical research. After this system is developed, it will serve as a first platform of its kind that can be later commercialized, which would help spur industry growth. To vitalize and enable high-tech/biotech companies to this {REDACTED} area {REDACTED}, engaging industry involvement to this area is necessary. Supporting such activities would furthermore foster the opportunity for student internships with industry and well as afford the students opportunities in entrepreneurship. Our institution is a Hispanic-serving undergraduate institute with almost 50% minority students. Such a proposed system is vital for promoting both the diversity and research culture {REDACTED} and will be leveraged extensively in outreach programs to encourage underrepresented minorities in science education and training. By actively reaching out to specific students who would particularly benefit from our proposed undergraduate internship program, we can attract at-risk students to engage them in research to promote their retention.
